UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/554,567	09/01/2000	Adriano Aguzzi	6458.US.01	2914

7590 12/10/2004

Steven F Weinstock
Abott Laboratories
100 Abbott Park Road
D 377 AP6D
Abbott Park, IL 60064-6050

EXAMINER	
WINKLER, ULRIKE	

ART UNIT	PAPER NUMBER
1648	

DATE MAILED: 12/10/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/554,567	AGUZZI ET AL.	
	Examiner	Art Unit	
	Ulrike Winkler	1648	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *August 3, 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *35-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *35-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 3, 2004 has been entered.

The amendment filed August 3, 2004 in response to the Office Action of November 14, 2003 is acknowledged and has been entered. Claims 35-37 are pending and are currently being examined.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Rejections - 35 USC § 103

The rejection of claims 35-37 under 35 U.S.C. 103(a) as being unpatentable over O'Rourke et al. (US Pat No. 6,165,784),and/or Korth et al. (Nature 6 November 1997; 390:74-77), in view of Kuroda et al. (Infection and Immunity 1983; 41:154-61) and/or Manuelidis et al. (Science 1978; 200:1069-1071) **is maintained** for reasons of record.

Applicants' arguments have been fully considered but have failed to persuade the Office to remove the instant rejection. Applicants' arguments are that the cited references of Kuroda et al. or Manuelidis et al. referred to the disease causing agent as being a virus instead of the instantly claimed prion protein (TSE infecting agent). The protein only theory of disease has only recently gained acceptance in the scientific community. The biochemist, Stanley Prusiner,

whose discovery provided key insights into dementia-related diseases, won the 1997 Nobel Medicine Prize, Sweden's Karolinska Institute. The institute said Prusiner's work helped the world to understand more about Alzheimer's and Mad Cow disease through his discovery of the prion, a disease-causing agent like bacteria or viruses. Even today there are is still a small group scientists that do not believe the protein only theory. Both of the cited references were published at a time when the prion protein theory of disease was not generally accepted. Even if the references erroneously referred to the disease-causing agent as a virus this does not detract from the important observation made in the references.

In response to Applicant's argument that there is no suggestion to combine the references, the examiner recognizes that obviousness can only be established by combining or modifying the teachings of the prior art to produce the claimed invention where there is some teaching, suggestion, or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art. See *In re Fine*, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988)and *In re Jones*, 958 F.2d 347, 21 USPQ2d 1941 (Fed. Cir. 1992). In this case, the animal experiments show that the disease causing agent is found in B and T cells of infected animals. The method of detecting the infecting agent in the experiments was to inject the fractionated sample into disease free animals. The experiments clearly show that the disease-causing agent is present in the T and B cells. The two other references disclose using a different method of detecting the disease-causing agent, with antibodies. This method of detection is direct, takes less time and does not require lengthy incubations.

Kuroda et al. fractionated B cells and T cells from diseased animals and inoculated the fractionated samples into non-diseased animals. The experiments indicate that the disease

causing agent obtained from the spleens of mice infected with the causative agent of Creutzfeldt-Jakob disease (CJD), can be injected into susceptible mice and transmit disease (see entire document, especially Tables 2 and 4). Thus Kuroda et al. teach a method to test for the presence of TSE byobtaining a sample of spleen, collecting B cells and T cells from the sample, and testing the B cells and/or T cells for the presence of the TSE agent.

Manuelidis et al. in 1978 established that collecting B cells and T cells from infected animals, by isolating the buffy coat, and injecting the buffy coat into disease free animals the animals came down with the disease. This established directly that the disease-causing agent is found in the buffy coat of blood. The reference also indicated that the hematogenous spread is implicated in man (see last paragraph).

O'Rourke et al. tests for TSE in lymphoid tissue using an antibody that serves as a ligand in various immunoassays, including immunohistochemistry, western immunoblots, and dot blots (see entire document, e.g., "Summary of the Invention"). O'Rourke et al. teach that antibody ligands may be either polyclonal sera or monoclonal antibodies (see entire document, e.g., column 5, especially lines 40-50). TSE containing aliquots equivalent to 125 mg starting material were electrophoresed through a 15% polyacrylamide mini-gel and transferred to PVDF membranes. The filters were developed with monoclonal antibody or a control antibody, goat anti-mouse IgG-HRPO, and a chemiluminescent substrate (see column 10, lines 34-65).

Korth et al. detects TSE based upon a monoclonal antibody that is specific for the prion form of PrP (the causative agent in TSEs) versus the cellular form of PrP (see entire document, e.g. Abstract). Korth et al. teach that this antibody can be used to identify the prion form of PrP directly, thus providing a basis for a TSE test in living humans or animals, by lowering the

detection threshold needed (see especially paragraph preceding "Methods" on page 77). Thus Kuroda et al. teach that both B cells and T cells can transmit TSE, and Manuelidis et al. teach that it is important to focus on these cellular populations to increase the sensitivity of assays for TSE infectivity.

Both O'Rourke et al. and Korth et al. teach methods of detecting the disease form of prion protein after proteinase K digestion followed by SDS-Page electrophoresis and blotting onto a membrane. One of ordinary skill in the art would have had a high expectation of success in applying the techniques taught by O'Rourke et al. or Korth et al. to the infected tissue disclosed by Kuroda et al. or Manuelidis et al. It would have been obvious at the time the invention was made to improve the sensitivity of the TSE tests by collecting samples containing B cells and/or T cells and testing for the presence of TSE using an antibody-based system. The ordinary artisan at the time the invention was made would have been motivated to this in order to avoid having to utilize animals in order to test for infectivity in the B and/or T cell population. The ordinary artisan at the time the invention was made would have reasonably expected that concentrating a cell type known to be infected with the TSE agent would increase the sensitivity of detection assays, including antibody-based assays. In addition, it was well known in the art at the time the invention was made that once an antibody was developed, the antibody could be used with a reasonable expectation of success to detect an antigen on intact cells, as in a buffy coat of whole blood, by either mounting them on slides for immunohistochemical analysis; or by using other techniques well known in the art at the time the invention was made for intact cell analysis with antibodies. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

Claim Rejections - 35 USC § 112

The rejection of claims 35-37 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement **is withdrawn** in view of Applicants' amendments to the claims.

The rejection of claims 35-37 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention **is withdrawn** in view of Applicants' amendments to the claims.

Conclusion

No claims allowed.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG (November 15, 1989). The Group 1600 Official Fax number is: (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Tech Center representative whose telephone number is (571)-272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ulrike Winkler, Ph.D. whose telephone number is 571-272-0912. The examiner can normally be reached M-F, 8:30 am - 5 pm. The examiner can also be reached via email [ulrike.winkler@uspto.gov].

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, James Housel, can be reached at 571-272-0902.

ULRIKE WINKLER, PH.D.
PRIMARY EXAMINER 12/9/04